

May 18, 2000

Novopharm NC Inc.
Attention: Dietrich Bartel
U.S. Agent for: Novopharm Limited
4700 Novopharm Blvd.
Wilson, NC 27893

Dear Sir:

This is in reference to your abbreviated new drug application dated December 16, 1993, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Terazosin Hydrochloride Tablets, 1 mg (base), 2 mg (base), 5 mg (base), and 10 mg (base).

Reference is also made to the Tentative Approval letters issued by this office to Novopharm Ltd. (Novopharm) on November 26, 1996 and December 29, 1999, and to your amendment dated March 17, 2000.

The reference listed drug product (RLD) cited in your application, Hytrin Tablets of Abbott Laboratories Pharmaceutical Products Division, is subject to periods of patent protection which expire on April 29, 2013 (U.S. Patents No. 5,504,207 [the '207 patent] and 5,412,095 [the '095 patent]) and February 17, 2000 (U.S. Patent No. 4,251,532 [the '532 patent]). With the exception of the '207 patent, all regulatory issues pertaining to these patents were resolved in Novopharm's favor upon issuance of the agency's tentative approval letter dated November 26, 1996. Furthermore, Novopharm Limited made an additional patent certification under Section 505(j)(2)(A)(vii)(IV) of the Act stating that your manufacture, use or sale of this drug product will not infringe the '207 patent, or that the '207 patent is invalid or unenforceable. Section 505(j)(5)(B)(iii) of the Act provides that approval of an abbreviated application shall be made effective immediately unless an action for patent infringement is brought before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received by the owner of the new drug application (NDA) for the reference listed drug product (Hytrin Tablets) and the patent holder. You have notified the agency that Novopharm Limited has complied with the requirements of Section 505(j)(2)(B) of the Act and that Abbott Laboratories

initiated a patent infringement suit against Novopharm Limited in the United States District Court for the Northern District of Illinois - Eastern Division [Abbott Laboratories vs. Novopharm Limited, Civil Action No. 96C-5868 (N.D. III)]. You have also notified the agency that the U.S. district Court ruled **in** Novopharm's favor and that Abbott's appeal to the U.S. Court of Appeals for the Federal Circuit affirmed the lower court's decision on July 1, 1999. Your undated correspondence received by this office on November 17, 1999 summarizes these findings and concludes that the '207 patent no longer precludes approval of Novopharm's application for terazosin hydrochloride tablets.

Furthermore, the Act provides that an abbreviated application that contains a certification described in section 505(j)(2)(A)(vii)(IV) (a Paragraph IV Certification) and that is for a drug for which a previous abbreviated application has been submitted, that also contains a Paragraph IV Certification, shall be made effective not earlier than one hundred and eighty days after:

1. the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or
2. the date of a decision of a court holding the patent which is the subject of the certification to be invalid or not infringed, whichever event occurs first {Section 505(j)(5)(B)(iv)}.

As noted in the Agency's publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations" (the "Orange Book"), an abbreviated new drug application for this drug product was approved for Geneva Pharmaceuticals Inc. (Geneva) on December 31, 1998. This application also contained a Paragraph IV Certification and was the first application received by the Agency for this drug product. Consequently, Geneva became eligible for 180 days of market exclusivity commencing on the date of first commercial marketing. However, Geneva did not market their product, and on March 23, 2000, Geneva notified the Agency that they were relinquishing any period of exclusivity to which they were entitled.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use

as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Terazosin Hydrochloride Tablets 1 mg (base), 2 mg (base), 5 mg (base) and 10 mg (base) to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Hytrin® Tablets, 1 mg (base), 2 mg (base), 5 mg (base) and 10 mg (base), respectively, of Abbott Laboratories Pharmaceutical Products Division). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

Under section 506A of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

Gary Buehler
Acting Director
Office of Generic Drugs
Center for Drug Evaluation and
Research

